נובמבר 2021

רופא/ה, רוקח/ת נכבד/ה,
חברת טבע מודיעה על עדכון עלון לרופא:

CIPRO-TEVA 2 MG/ML
SOLUTION FOR INFUSION

ציפרו-טבע 2 מ"ג/מ"ל
תמיסה למתן בעירוי

(1 ml solution for infusion contains: 2 mg ciprofloxacin (as lactate))

<u>התוויה כפי שאושרה בתעודת הרישום:</u>

<u>Adults:</u>
Broad spectrum antibiotic for infections caused by ciprofloxacin sensitive pathogens.

<u>Children and adolescents:</u>

- Broncho-pulmonary infections in cystic fibrosis caused by Pseudomonas aeruginosa
- Complicated urinary tract infections and pyelonephritis
- Inhalation anthrax (post-exposure prophylaxis and curative treatment)

Ciprofloxacin may also be used to treat severe infections in children and adolescents when there is no other alternative.

Treatment should be initiated only by physicians who are experienced in the treatment of cystic fibrosis and/or severe infections in children and adolescents.

עדכונים בעלון לרופא

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ברצוננו להודיע שהעלון לרופא עודכן, בפירוט שלהלן כלולים העדכונים העיקריים בלבד (תוספות מסומנות באדום והסרות מידע כטקסט מחוק):

4.4 Special warnings and precautions for use

[...]

<u>Urinary tract infections</u>

<u>Resistance to fluoroquinolones of *Escherichia coli* - the most common pathogen involved in urinary tract infections - varies across the European Union. Prescribers are advised to take into account the local prevalence of resistance in *Escherichia coli* to fluoroquinolones.</u>

[...]

Complicated urinary tract infections and pyelonephritis
Ciprofloxacin treatment of urinary tract infections should be considered when other treatments cannot be used, and should be based on the results of the microbiological documentation.
Clinical trials have included children and adolescents aged 1-17 years.

Other specific severe infections
Other severe infections in accordance with official guidance, or after careful benefit-risk evaluation when other treatments cannot be used, or after failure to conventional therapy and when the microbiological documentation can justify a ciprofloxacin use.

The use of ciprofloxacin for specific severe infections other than those mentioned above has not been evaluated in clinical trials and the clinical experience is limited. Consequently, caution is advised when treating patients with these infections.

Hypersensitivity
Hypersensitivity and allergic reactions, including anaphylaxis and anaphylactoid reactions, may occur following a single dose (see section 4.8) and may be life-threatening. If such reaction occurs, ciprofloxacin should be discontinued and an adequate medical treatment is required.

Prolonged, disabling and potentially irreversible serious adverse drug reactions
Very rare cases of prolonged (continuing months or years), disabling and potentially irreversible serious adverse drug reactions affecting different, sometimes multiple, body systems (musculoskeletal, nervous, psychiatric and senses) have been reported in patients receiving quinolones and fluoroquinolones irrespective of their age and pre-existing risk factors. Ciprofloxacin should be discontinued immediately at the first signs or symptoms of any serious adverse reaction and patients should be advised to contact their prescriber for advice.
[...]

Patients with myasthenia gravis
Ciprofloxacin should be used with caution in patients with myasthenia gravis, because symptoms can be exacerbated (see section 4.8).

Aortic aneurysm and dissection, and heart valve regurgitation/incompetence
Epidemiologic studies report an increased risk of aortic aneurysm and dissection, particularly in elderly patients, and of aortic and mitral valve regurgitation after intake of fluoroquinolones. Cases of aortic aneurysm and dissection, sometimes complicated by rupture (including fatal ones), and of regurgitation/incompetence of any of the heart valves have been reported in patients receiving fluoroquinolones (see section 4.8).

Therefore, fluoroquinolones should only be used after careful benefit-risk assessment and after consideration of other therapeutic options in patients with positive family history of aneurysm disease or congenital heart valve disease, or in patients diagnosed with pre-existing aortic aneurysm and/or dissection or heart valve disease, or in

presence of other risk factors or conditions predisposing:

- for both aortic aneurysm and dissection and heart valve regurgitation/incompetence (e.g. connective tissue disorders such as Marfan syndrome or Ehlers-Danlos syndrome, Turner syndrome, Behcet's disease, hypertension, rheumatoid arthritis) or additionally
- for aortic aneurysm and dissection (e.g. vascular disorders such as Takayasu arteritis or giant cell arteritis, or known atherosclerosis, or Sjogren's syndrome) or additionally
- for heart valve regurgitation/incompetence (e.g. infective endocarditis).

The risk of aortic aneurysm and dissection, and their rupture may also be increased in patients treated concurrently with systemic corticosteroids.
In case of sudden abdominal, chest or back pain, patients should be advised to immediately consult a physician in an emergency department.
Patients should be advised to seek immediate medical attention in case of acute dyspnoea, new onset of heart palpitations, or development of oedema of the abdomen or lower extremities.
[...]

4.5 Interactions with other medicinal products and other forms of interaction
[...]

Agomelatine
In clinical studies, it was demonstrated that fluvoxamine, as a strong inhibitor of the CYP450 1A2 isoenzyme, markedly inhibits the metabolism of agomelatine resulting in a 60-fold increase of agomelatine exposure. Although no clinical data are available for a possible interaction with ciprofloxacin, a moderate inhibitor of CYP450 1A2, similar effects can be expected upon concomitant administration (see section 4.4).

Zolpidem
Co-administration of ciprofloxacin may increase blood levels of zolpidem, concurrent use is not recommended
[...]

4.8 Undesirable effects

System/ organ class	**Common ≥ 1/100 to < 1/10**	**Uncommon ≥ 1/1,000 to < 1/100**	**Rare ≥ 1/10,000 to < 1/1,000**	**Very rare < 1/10,000**	**Frequency unknown (cannot be estimated from the available data)**
Endocrine disorders					Syndrome of inappropriate secretion of antidiuretic hormone (SIADH

System/ organ class	Common ≥ 1/100 to < 1/10	Uncommon ≥ 1/1,000 to < 1/100	Rare ≥ 1/10,000 to < 1/1,000	Very rare < 1/10,000	Frequency unknown (cannot be estimated from the available data)
Metabolism and Nutrition disorders		Anorexia Decreased appetite	Hyper-glycemia Hypoglycaemia (see section 4.4)		Hypo-glycaemic coma (see section 4.4)
Psychic Disorders*		Psychomotor hyperactivity / agitation	Confusion and disorientation Anxiety reaction Abnormal dreams Depression (potentially culminating in suicidal ideations/thoughts or suicide attempts and completed suicide) (see section 4.4) Hallucinations	Psychotic reactions (potentially culminating in suicidal ideations/thoughts or suicide attempts and completed suicide) (see section 4.4)	Mania, incl. hypomania
[...]					
Cardiac Disorders**			Tachycardia		Ventricular arrhythmia and torsades de pointes (reported predominantly in patients with risk factors for QT prolongation), ECG QT prolonged (see Section 4.4 and 4.9)
Vascular disorders**			Vasodilation Hypotension Syncope	Vasculitis	
[...]					
Gastro-intestinal disorders	Nausea Diarrhoea	Vomiting Gastro-intestinal and	Antibiotic-associated colitis (very	Pancreatitis	

System/ organ class	Common ≥ 1/100 to < 1/10	Uncommon ≥ 1/1,000 to < 1/100	Rare ≥ 1/10,000 to < 1/1,000	Very rare < 1/10,000	Frequency unknown (cannot be estimated from the available data)
		abdominal pain Dyspepsia Flatulence	rarely with possible fatal outcome) (see section 4.4)		
[...]					
Skin and subcutaneous tissue disorders		Rash Pruritus Urticaria	Photo-sensitivity reactions (see section 4.4)	Petechiae Erythema multiforme Erythema nodosum Stevens-Johnson Syndrome (potentially life threatening) Toxic epidermal necrolysis (potentially life threatening)	Acute generalised exanthematous pustulosis (AGEP) Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)
[...]					

The most commonly reported adverse drug reactions (ADRs) are nausea, diarrhoea, vomiting, transient increase in transaminases, rash, and injection and infusion site reactions.
[...]

*Very rare cases of prolonged (up to months or years), disabling and potentially irreversible serious drug reactions affecting several, sometimes multiple, system organ classes and senses (including reactions such as tendonitis, tendon rupture, arthralgia, pain in extremities, gait disturbance, neuropathies associated with paraesthesia, depression, fatigue, memory impairment, sleep disorders, and impairment of hearing, vision, taste and smell) have been reported in association with the use of quinolones and fluoroquinolones in some cases irrespective of preexisting risk factors (see section 4.4).

**Cases of aortic aneurysm and dissection, sometimes complicated by rupture (including fatal ones), and of regurgitation/incompetence of any of the heart valves have been reported in patients receiving fluoroquinolones (see section 4.4).

[...]

העלון לרופא נשלח לפרסום במאגר התרופות שבאתר האינטרנט של משרד הבריאות וניתן לקבלו מודפס ע"י פניה לחברת טבע. http://www.health.gov.il